UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/486,247	05/25/00	DEAR	T 8484-081-999

HM22/1023

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EXAMINER	
FRONDA,C	
ART UNIT	**PAPER NUMBER**
1652	14

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/486,247	Dear et al.
Examiner	**Art Unit**
Christian L. Fronda	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *8, 9, 16, and 17* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *8, 9, 16, and 17* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. In the **AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT** dated September 12, 2001 (Paper No. 11), Applicants have canceled claims 1-7 and 10-15 and added new claims 16 and 17.

Election/Restrictions

2. Applicants' election with traverse of Group V, claims 8 and 9, in Paper No. 11 is acknowledged. The traversal is on the grounds that the subject matter of Group V and Group VI merit examination because the claims of Group V are directed toward a method of administering a compound and the dependent claims of Group VI are directed toward the same method except for administering one or more additional substances. This is not found persuasive because the processes of Groups V and VI are distinct both physically and functionally; and require different process steps, reagents, and parameters. Furthermore, the inventions of Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the reasons stated in the Office Action dated July 11, 2000 (Paper No. 9).

The requirement is still deemed proper and is therefore made FINAL.

3. Elected claims 8 and 9 and new claims 16 and 17 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 8, 9, 16, and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of claims encompass a method for the "negative regulation of the keratinization of hair" comprising administration of any "protease-related protein" comprising an amino acid sequence that differs from SEQ ID NO:2 "by one or more amino acids" or is encoded by a polynucleotide which differs from SEQ ID NO: 1 by "one or more base pairs". The specification provides guidance and examples for making a protease consisting of the amino acid sequence of SEQ ID NO: 2 or encoded by the polynucleotide consisting of SEQ ID NO: 1. While molecular biological techniques and genetic manipulation techniques are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific amino acid residue(s) or base pairs to add, delete, substitute, or combinations thereof in SEQ ID NO: 2 or SEQ ID NO: 1, respectively, to make a protein that still retains protease activity is lacking. Thus, searching for the specific amino acid residue(s) or base pairs to add, delete, substitute, or combinations thereof in SEQ ID NO: 2 or SEQ ID NO: 1, respectively, to make a protein that still retains protease activity is well outside the realm of routine experimentation and predictability in the art of success is extremely low.

The amount of experimentation to the specific amino acid residue(s) or base pairs to add, delete, substitute, or combinations thereof in SEQ ID NO: 2 or SEQ ID NO: 1, respectively, to make a protein that still retains protease activity is enormous. Such experimentation entails selecting specific amino acid residue(s) to add, delete, substitute, or combinations thereof in SEQ ID NO: 2, mutating the DNA encoding SEQ ID NO: 2 to have the selected mutations, expressing the mutants, and screening for mutants that still retain protease activity. Since routine experimentation in the art does not include making and screening vast numbers of mutants that have "an amino acid sequence differing therefrom by one or more amino acids" or are encoded by a polynucleotide that differs from SEQ ID NO: 1 by "one or more base pairs" and still retain protease activity, where the expectation of obtaining a desired protein having protease activity and an amino acid sequence differing from SEQ ID NO: 2 by "one or more amino acids" or encoded by a polynucleotide that differs from SEQ ID NO: 1 by "one or more base pairs" is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific amino acid residue(s) to add, delete, substitute, or combinations thereof to SEQ ID NO: 2. Without such a guidance, the experimentation left to those skilled in the art is undue.

While the specification discloses administering the claimed "protease-related protein" would be used in the "negative regulation of the keratinization of hair", the specification fails to

demonstrate a distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair"and that administration of the claimed "protease-related protein" to a patient does not harm the patient. Thus, searching for distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair"and that administration of the claimed "protease-related protein" to a patient does not harm the patient is well outside the realm of routine experimentation and predictability in the art of success in determining a distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair"is extremely low.

The amount of experimentation to determine a distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair"and that administration of the claimed "protease-related protein" to a patient does not harm the patient is enormous and entails searching for a causal relationship between the claimed "protease-related protein" and the "keratinization of hair"and determining whether administration of the claimed "protease-related protein" to a patient does not harm the patient and results in the "negative regulation of the keratinization of hair".

Since routine experimentation in the art does not include determining a distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair" and that administration of the claimed "protease-related protein" to a patient does not harm the patient, where the expectation of determining a distinct and well defined relationship between the claimed "protease-related protein" and the "keratinization of hair" is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the causal relationship between the claimed "protease-related protein" and the "keratinization of hair". Without such a guidance, the experimentation left to those skilled in the art is undue.

Administering a "therapeutically effective amount" of the claimed "protease-related protein" in the absence of in vivo data is unpredictable because (1) the peptide/polypeptide may be inactivated before producing an effect due to proteolytic degradation or immunological inactivation or the inherently short half-life of the peptide/polypeptide; (2) the peptide/polypeptide may not reach the target area because, i.e. the peptide/polypeptide may not be able to cross the mucosa or the peptide/polypeptide may be adsorbed by fluids, cells and tissues where the peptide/polypeptide has no effect; and (3) other functional properties, known or unknown, may make the peptide/polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects which prohibit the use of the peptide for the "negative regulation of the keratinization of hair". See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Since there is no in vivo working examples in the specification as filed to demonstrate the "negative regulation of the keratinization of hair" by administering the claimed "protease-related protein", it is not clear that the claimed method is enabled. In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates

that the more unpredictable the area is, the more specific enablement is necessary.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 8, 9, 16, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 8, the phrase "a protease-related protein" renders the claim indefinite because the meaning of the phrase is not known and it is not known when a protein is or is not related to a protease. Thus, one of skill in the art cannot determine the metes and bounds of the claimed invention.

In claim 9, the phrase "wherein the protein is present as such or in the form of a nucleic acid" renders the claim indefinite because a protein is a polymer of amino acid residues not a polymer of nucleotide. Claims 16 and 17 which depend from claim 9 are also rejected because they do not correct the defect of claim 9.

In claims 16 and 17, the phrase "a DNA hybridizing" renders the claims indefinite because the specific hybridization conditions are not recited in the claims.

In claims 16 and 17, the phrase "via the degenerated genetic code" renders the claim indefinite because the meaning of the phrase is not known and it is not known when a DNA is or is not related to the claimed DNA "via the degenerated genetic code".

Conclusion

8. No claim is allowed.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Meier et al. teach a serine protease overexpressed in the hair follicles of nude mice.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

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